REMARKS

Reconsideration of this application, as amended, is respectfully requested.

Claims 44-48, 73, and 75-77 and 81-82 are pending. Claims 78-80 are now canceled without prejudice or disclaimer. Applicants hereby explicitly preserve the rights to pursue all canceled subject matter in one or more future applications. Claims 44 and 47 are amended to further clarify the scope of the claimed invention or to correct informalities. The amendments are fully supported by the originally filed specification and claims, for example, on page 10, third paragraph; page 11, first paragraph; page 21, second paragraph step (c); page 21, last paragraph to page 22, fourth paragraph; Examples 2-5 and claim 42 as originally filed. Thus, the amendments do not constitute new matter.

A. Priority

Applicants thank the Office for acknowledging this application as a proper National Stage entry of PCT Application No. PCT/EP99/04310, and for acknowledging the priority claim to German Application No. 198 27 714.8 filed on June 22, 1998 and to German Application No. 198 38 802.0 filed August 26, 1998. The Office has acknowledged that the certified copies of these two priority documents have been received.

B. Terminal Disclaimer

The Examiner disapproves the terminal disclaimer filed November 14, 2008 as being improper, because the terminal disclaimer was allegedly not signed by an attorney or agent acting in a representative capacity as provided by 37 C.F.R. §§ 1.34(a), 1.321(b) and/or(c). Applicants respectfully submit that the undersigned practitioner was associated with the Customer Number 020306 at the time the terminal disclaimer was filed, November 14, 2008. However, the Office's records failed to correctly reflect such. Applicants have contacted the Office and have been assured by the Office that the records have been corrected.

Thus, Applicants hereby request reconsideration and entry of the terminal disclaimer previously filed and reapplication of the fee previously paid on November 14, 2008. Since the terminal disclaimer fee has been paid, no further terminal disclaimer fee is due in connection with this filing.

C. Claim Objections

The Action objects to claim 47 for lacking a period at the end of the claim. Applicants thank the Examiner for pointing out the informalities and have amended claim 47 accordingly to obviate the objection. Thus, the objection is now moot.

D. Rejections under 35 U.S.C. §112, First Paragraph, Written Description

Claims 44-48, 73, 75-80 stand rejected for allegedly failing to comply with the written description requirement under 35 U.S.C. § 112, first paragraph. Specifically, the Examiner asserts that the recitation of an "inert solid phase" in claim 44 steps (a) and (d) lacks sufficient written support.

Applicants traverse the rejection but have nevertheless amended claim 44 steps (a) and (d) to cancel the term "inert solid phase." Thus, the amendment has rendered the rejection moot.

E. Rejections under 35 U.S.C. §112, Second Paragraph

The Action rejects Claims 44-48, 73, 75-80 for alleged being indefinite under 35 U.S.C. § 112, second paragraph. Specific rejections are listed below.

In paragraph 14, the Action rejects claim 44 because the recitation of the term "derived from" is allegedly unclear. Specifically, the Action asserts that the term "derived from" is undefined, and, although both HIV antigens and antibodies specific for the antigens are disclosed, it is unclear by what process(es) the analytes would be "derived."

Applicants traverse the rejection but have nevertheless amended the claims. Claim 44 as amended recites "wherein the plurality of analytes is at least two analytes selected from the group consisting of proteins of the pathogen and antibodies specific for the proteins," the disclosure of which has been acknowledged by the Examiner. See page 7, paragraph 14 of the Office Action. Applicants submit that the amendment has rendered the rejection moot.

In paragraph 15, Claim 44 stands rejected because it is allegedly unclear how the "test area-specific background" recited in step (d) is specific for a particular test area. Claim 44, step (d), as amended, recites: "wherein the test area-specific background is detected from a signal

generated by any signal-generating group non-specifically bound to the at least first or second test area in the absence of any analyte of the plurality of analytes." Applicants submit that the claim clearly defines how the test area-specific background is related to each test area: the test area-specific background for the first test area is measured from any non-specific binding on the first test area in the absence of the plurality of analytes, and the test area-specific background for the second test area is measured from any non-specific binding on the second test area in the absence of the plurality of analytes. Thus, the metes and bounds of the claim are clear. Reconsideration and withdrawal of the rejection is requested.

In paragraph 16, Claim 47 is rejected because the recitation to "the solid phase" purportedly lacks proper antecedent basis. Applicants submit that amendment made to claim 44 removing the term "an inert solid phase" has rendered the rejection moot.

F. Rejections under 35 U.S.C. § 102

The Action rejects Claim 44-45, 47-48, 73, 76-79 and 81 under 35 U.S.C. § 102(a) as being unpatentable over Karl et al. (WO 99/05525, the English disclosure of which is based on US 6,815,217 as alleged by the Office) (hereinafter "Karl"). Specifically, the Action asserts that Karl teaches detecting a plurality of analytes derived from a pathogen in a sample using a solid phase having at least one spatially discrete test area and at least one control area for detecting nonspecific binding. The Action asserts that the control area taught in Karl is considered an inert solid phase because it does not react with the analyte. The Action further asserts that Karl teaches a test area-specific cut-off index (COI) based on the disclosure of col. 5, line 66 to col. 6, line 45.

Applicants respectfully submit that both WO 99/05525 and US 6,815,217 ("the '217 patent") are disqualified as prior art under the provisions of 35 U.S.C. § 102. WO 99/05525 was published on February 4, 1999 and was cited as prior art under 35 U.S.C. § 102(a) by the Office. The instant application is a U.S. National Stage entry of PCT Application No. PCT/EP99/04310, filed June 22, 1999. The instant application is entitled to the priority dates of June 22, 1998, the filing date of German Application No. 198 27 714.8, and August 26, 1998, the filing date of German Application No. 198 38 802.0. Both of the priority dates predate the publication date of WO 99/05525. Thus, WO 99/05525 is disqualified as prior art with respect to the instant

application. Pursuant to M.P.E.P. § 201.15, copies of the English translation of the two German Applications are submitted with this response for the Examiner's review, and a statement indicating that the translation of the certified copies are accurate is also attached.

In addition, the 217 patent is disqualified under 35 U.S.C. §§ 102(a) or (b) because it was published after the filing date of the instant application. The 217 patent is also disqualified as prior art under 35 U.S.C. § 102(e) because its effective U.S. filing date for prior art purpose, i.e., its § 371 (c)(1), (2), (4) date, is January 21, 2000, after the filing date of the instant application.

Thus, neither WO 99/05525 nor the 217 patent are prior art under 35 U.S.C. § 102. Reconsideration and withdrawal of the rejection under 35 U.S.C. § 102(a) over Karl is respectfully requested.

G. Rejections under 35 U.S.C. §103(a)

The Action raises several rejections under 35 U.S.C. § 103(a) of claims 44-48, 73, 75-80 as being obvious. Specific rejections are listed below.

1. Claim rejection under 35 U.S.C. § 103(a) based on Karl

In paragraph 20, Claim 46 is rejected under 35 USC § 102(a) as anticipated by or, in the alternative, under 35 USC § 103(a) as obvious over Karl. Specifically, the Action asserts that Karl teaches that the test areas most preferably have a diameter of 0.01 mm to 2 mm, which largely overlaps the range of 0.01 mm to 1 mm recited in claim 46. The Action asserts that a *prima facie* case of obviousness exists because one of skill in the art would have arrived at the claimed range by routine optimization.

As stated above, Karl is disqualified as prior art. Thus, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 103(a) based on Karl.

2. Claim rejection under 35 U.S.C. § 103(a) based on Karl in view of Ohkawa, Ohnishi, Hyman, Chan, Lesniewski, Kiyosawa, and Yuki

In paragraph 21, claim 80 is rejected as being unpatentable over Karl in view of Ohkawa et al. (J. Hepatol. 1994, 21:509-14) ("Ohkawa"), Ohnishi et al. (Gastroentero Jpn. 1991, Suppl. 3:212-5) ("Ohnishi"), Hyman et al. (US 5,384,240) ("Hyman"), Chan et al. (US 5,120,662) ("Chan"), Lesniewski et al. (US 6,596,476) ("Lesniewski"), Kiyosawa et al. (Gastroenterol. Jpn.

1986, 21:601-7) ("Kiyosawa"), and Yuki et al. (Hepatology, 1995, 22:402-6) ("Yuki"). Applicants traverse the rejection but submit that the cancelation of claim 80 has rendered the rejection moot.

3. Claim rejection under 35 U.S.C. § 103(a) based on O'Connor

In paragraph 22, claims 44-45, 47-48, 73, 75-77 and 81 stand rejected under 35 U.S.C. § 103(a) over O'Connor et al. (U.S. 5,627,026) ("O'Connor"). Specifically, the Action asserts that O'Connor teaches a solid support containing a first location with an antigen capable of selectively forming an immune complex with a sample antibody bound thereto, and a second location with an antibody capable of selectively forming an immune complex with a sample antigen bound thereto. The Action further asserts that O'Connor discloses measuring signals from the negative controls, in which antigen-coated wells were contacted with samples known not to contain analyte and the absorbance intensity of each well was compared to the negative control. Such comparisons are allegedly "test area-specific" as they involved comparing signals in each teat area with that of the negative control. Applicants traverse the rejection.

A claimed invention is unpatentable if the differences between it and the prior art "are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art." 35 U.S.C. § 103(a); *see Graham v. John Deere Co.*, 383 U.S. 1, 14 (1966). The ultimate determination of whether an invention is or is not obvious is based on underlying factual inquiries including: (1) determining the scope and content of the prior art; (2) ascertaining the differences between the prior art and the claims at issue; (3) resolving the level of ordinary skill in the pertinent art; and (4) evaluating evidence of secondary considerations. *See Graham*, 383 U.S. at 17-18.

The Supreme Court emphasizes that the key of supporting any rejection under 35 U.S.C. §103 is the clear articulation of the reason(s) why the claimed invention would have been obvious. *KSR Int'l Co. v. Teleflex Inc.*, 127 U.S. 1727, 1741 (2007). The Court, quoting *In re Kahn*, stated that "rejections on obviousness cannot be sustained with mere conclusory statements; instead, there must be some articulated reasoning with some rational underpinning to support the legal conclusion of obviousness." *In re Kahn*, 441, F.3d 977, 988 (Fed. Cir. 2006).

Contrary to the claimed method, O'Connor teaches a detection method wherein the negative control spot is a specifically designated negative control spot distinct from the sample

spot. See col. 5, lines 59-61. Even if, as asserted in the Action, O'Connor alludes to a solid support containing multiple test spots each for detecting a different analyte, the solid support contains a common negative control spot to which all test spots are compared. See col. 5, lines 6-9 and the Figure. O'Connor does not teach a test area-specific background measured by detecting signals generated by any signal-generating group non-specifically bound to the *at least first or second test area* in the absence of any analyte of the plurality of analytes. Further, O'Connor does not teach separately detecting a test area-specific background for each test area, and thus for each analyte – the background signal of the common control area would have to be used as the background levels for ALL test areas, and thus for all analytes.

Further, O'Connor does not teach a test area-specific cut-off for each analyte. In O'Connor, the presence or absence of an analyte is determined by relating the optical density value of the sample on different test spots to the common negative control. "Anything 3 times greater in absorbance intensity than the negative control is regarded as a positive sample." See col. 9, lines 23-24. There is no teaching that the threshold or cut-off value for each test area, thus for each analyte, may be different and must be calculated individually. O'Connor does not recognize the drawbacks of using a common cut-off value for all analytes – the common cut-off is defined by the worst parameter, and can result in a specific but less sensitive assay. In extreme cases, replying on such a common cut-off value can lead to false negative results. The inventive concept of the claimed method where individually calculated test area-specific cut-offs enable high sensitivity while maintaining high specificity in an assay is entirely missing in O'Connor. Thus, the claimed method as recited in claim 44 and dependent claims 45, 47-48, 73, 75-77 and 81 would not have been obvious to one of ordinary skill in the art based on O'Connor.

4. Claim rejection under 35 U.S.C. § 103(a) based on O'Connor in view of Ekins

In paragraph 23, claim 46 stands rejected under 35 U.S.C. § 103(a) as unpatentable over O'Connor in view of Ekins (U.S. 5,837,551). Specifically, the Action asserts that while O'Connor does not teach a test area with a diameter of 0.01- 1 mm, Ekins teaches microspots with diameter of 80 microns or 0.08 mm.

Applicants traverse the rejection. Claim 46 depends on claim 44. As discussed above, O'Connor does not teach detecting a test area-specific background for each different analyte, and does not teach calculating a test area-specific cut-off for each different analyte. Neither does

Ekins. O'Connor does not recognize the drawbacks of using a common cut-off, and does not provide motivation for modifying the method by calculating a test area-specific cut-off based on a test area-specific background detected from non-specific binding to the first or second test area in the absence of any analyte of the plurality of the analytes. Neither does Ekins. Ekins merely relates to the size of the test areas and certainly does not cure the defects. One of ordinary skill in the art would not have been motivated to modify O'Connor by the disclosures of O'Connor and/or Ekins to detect a test area-specific background by measuring non-specific bindings to each test area, and to separately calculate test area-specific cut-off based on the background of each test area. Thus, Applicants respectfully submit that claim 46 is not obvious over O'Connor in view of Ekins. Reconsideration and withdrawal of the rejection is thus respectfully requested.

5. Claim rejection under 35 U.S.C. § 103(a) based on O'Connor in view of Carpenter, and further in view of Ohkawa, Ohnishi, Hyman, Chan, Lesniewski, Kiyosawa, and Yuki

In paragraph 24, claims 78-80 are rejected under 35 U.S.C. § 103(a) as unpatentable over O'Connor in view of Carpenter ("Enzyme-linked immunoassays" In: Manual of Clinical Laboratory Immunology, Noel R. Rose et al. (Eds), ASM Press, Washington, DC (1997) 5th Ed., pp. 20-29)("Carpenter"), and further in view of Ohkawa, Ohnishi, Hyman, Chan, Lesniewski, Kiyosawa, and Yuki. Applicants traverse the rejection but submit that cancelation of claims 78-80 has rendered the rejection moot.

6. Claim rejection under 35 U.S.C. § 103(a) based on O'Connor in view of Miyamura or based on Karl, in view of O'Connor and Miyamura

In paragraph 25, claim 82 is rejected under 35 U.S.C. § 103(a) as unpatentable over O'Connor in view of Miyamura et al. (U.S. 5,714,314) ("Miyamura"), or in the alternative, as being unpatentable over Karl in view of O'Connor and Miyamura. Claim 82 depends on claim 44 and is directed to a method for detecting a pathogen by detecting a plurality of analytes, wherein the plurality of analytes is human hepatitis C virus (HCV) antibodies or antigens. As stated above, Karl is disqualified as prior art. Withdrawal of rejections based on Karl is requested. Only O'Connor and Miyamura are discussed.

Specifically, the Action asserts that while O'Connor does not teach detection of HCV antigens and antibodies, Miyamura teaches that prevention, early diagnosis and treatment of

HCV infection were important. Thus, the Action reasons that it would have been obvious to one of skill in the art to select HCV as the type of viral infection in the method for simultaneous assay for antigens and antibodies as taught by O'Connor.

Applicants traverse the rejection. Even if one of ordinary skill in the art would have chosen to detect HCV antigens and antibodies by using the method of O'Connor, claim 82 is not obvious because the O'Connor method does not teach the claimed test area-specific background and test area-specific cut-off.

Contrary to the claimed method, O'Connor teaches a detection method wherein the negative control spot is a specifically designated negative control spot distinct from the sample spot. See col. 5, lines 59-61. Even if, as alleged in the Action, O'Connor alludes to a solid support containing multiple test spots each for detecting a different analyte, the solid support contains a common negative control to which all test spots are compared. See col. 5, lines 6-9 and the Figure. O'Connor does not teach a test area-specific background measured by detecting signals generated by any signal-generating group non-specifically bound to the *at least first or second test area* in the absence of any analyte of the plurality of analytes. Further, O'Connor does not teach separately detecting a test area-specific background for each test area, and thus for each analyte – the background signal of the common control area is used as the background levels for ALL test areas, and thus for all analytes.

Further, O'Connor does not teach a test area-specific cut-off for each analyte. In O'Connor, the presence or absence of an analyte is determined by relating the optical density value of the sample on different test spots to the common negative control spot. "Anything 3 times greater in absorbance intensity than the negative control is regarded as a positive sample." See col. 9, lines 23-24. There is no teaching that the threshold or cut-off value for each test area, thus for each analyte, may be different and must be calculated individually. O'Connor does not recognize the drawback of using a common cut-off value for all analytes – the common cut-off value is defined by the worst parameter of the plurality of analytes and the use of a common cut-off can result in a specific but less sensitive assay. In extreme cases, replying on such a common cut-off value can lead to false negative results. The inventive concept of the claimed method where individually calculated test area-specific cut-offs enable high sensitivity while maintaining high specificity in an assay is completely missing in O'Connor. The claimed method thus would not have been obvious to one of ordinary skill in the art based on O'Connor, in view of Miyamura.

Based on the above, Applicants respectfully request reconsideration and withdrawal of the rejections under 35 U.S.C. § 103(a).

H. Double Patenting

In paragraph 27, claims 44-48, 73, and 75-77 stand rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-34 of the '217 patent in view of Schonbrunner (GB 2 313 666A). Additionally, in paragraph 28, claims 78-80 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-34 of the '217 patent in view of Schonbrunner, and further in view of Ohkawa, Ohnishi, Hyman, Chan, Lesniewski, Kiyosawa, and Yuki.

Applicants respectfully traverse the rejections but had nevertheless filed a terminal disclaimer with regard to the co-owned U.S. Patent No. 6,815,217. Applicants submit that the terminal disclaimer and the cancelation of claims 78-80 have rendered the double patenting rejections moot.

I. Conclusion

Reconsideration of this application is respectfully requested and a favorable determination is earnestly solicited. The Examiner is invited to contact the Applicants' undersigned representative at (312) 913-0001 if the Examiner believes that this would be helpful in expediting prosecution of this application.

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Respectfully,

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